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TABLE OF CONTENTS

Pathologic Diagnosis/Initial Evaluation.....	Page 2
Classic Hodgkin Lymphoma Stage I-II.....	Pages 3-4
Classic Hodgkin Lymphoma Advanced Stages III, IV.....	Pages 5-6
Lymphocyte Predominant Hodgkin Lymphoma.....	Page 7
Follow-up After Completion of Treatment.....	Page 8
Salvage Therapy.....	Page 9
APPENDIX A: Unfavorable Risk Factors for Stage I-II Classic Hodgkin Lymphoma.....	Page 10
APPENDIX B: Deauville Criteria/5-Point Scale (5PS).....	Page 10
APPENDIX C: Radiation Therapy Guidelines.....	Page 11
APPENDIX D: International Prognostic Score (Hasenclaver Index).....	Page 12
APPENDIX E: Systemic Therapy for Relapsed or Refractory Disease.....	Page 13
Suggested Readings.....	Pages 14-16
Development Credits.....	Page 17

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NOTE: Consider Clinical Trials as treatment options for eligible patients.

PATHOLOGIC DIAGNOSIS¹

ESSENTIAL:

- FNA alone is insufficient
- Hematopathology review of all slides with at least one tumor paraffin block. Re-biopsy if consult material is non-diagnostic. Core needle biopsy may be adequate if diagnostic, but an excisional nodal biopsy is recommended.
- Flow cytometry often not helpful
- Adequate immunophenotype to confirm diagnosis
 - Immunohistochemistry on paraffin panel for Hodgkin lymphoma (HL) including nodular lymphocyte predominant HL:
 - CD20, PAX-5, CD30, CD3, CD15, CD21, and CD45 (LCA)
 - EBER

OF USE IN CERTAIN CIRCUMSTANCES:

- Immunohistochemical studies:
 - LMP1
 - BOB1, OCT2, and CD79a (differential diagnosis with B-cell lymphoma, unclassifiable with features intermediate between classic HL and DLBCL and primary mediastinal large B-cell lymphoma).
 - CD23, or CD35 (follicular dendritic cell markers), BCL6 in cases of nodular lymphocyte predominant HL (may help with T-cell/histiocyte rich large B-cell lymphoma)
 - CD2, CD43, ALK (differential diagnosis with anaplastic large cell lymphoma)

STRONGLY RECOMMEND:

- Core biopsy for tissue banking by protocol

INITIAL EVALUATION

ESSENTIAL:

- History and physical including:
 - Alcohol intolerance
 - Pruritus
 - Exam of nodes
 - B symptoms (unexplained fever > 38°C during the previous month; Recurrent drenching night sweats during the previous month; Weight loss > 10% of body weight ≤ 6 months of diagnosis)
 - Performance Status
 - Fatigue
 - Size of spleen, liver
- CBC with differential, LDH, BUN, creatinine, albumin, AST, ALT, total bilirubin, alkaline phosphatase, serum calcium, uric acid
- Erythrocyte sedimentation rate (ESR)
- Screening for HIV 1, HIV 2, hepatitis B and C (HBcAb, HBsAg, HCVAb)
- PET/CT with contrast
- Pulmonary Function Tests
- Consider bone marrow biopsy if there are cytopenias and/or inconclusive PET
- MUGA scan or echocardiogram
- Counseling: psychosocial if clinically indicated
- Lifestyle risk assessment²
- Discuss fertility options and sperm banking for patients of child bearing potential (refer to [Fertility Preservation Prior to Cancer Treatment \(Women\) algorithm](#))

OF USE IN SELECTED CASES:

- Chest x-ray, PA and LAT
- Pregnancy test
- Cardiology consultation at baseline if risk factors for cardiac toxicity [e.g., obesity, abnormal echocardiogram, hypertension (HTN), hyperlipidemia (HLD)]

See [Pages 3-4](#):
 Classic Hodgkin Lymphoma Stage I-II

See [Page 5-6](#):
 Classic Hodgkin Lymphoma Advanced Stages III, IV

See [Page 7](#):
 Lymphocyte Predominant Hodgkin Lymphoma

¹ Review [MD Anderson approved biomarkers](#)

² See [Physical Activity, Nutrition, and Tobacco Cessation](#) algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice

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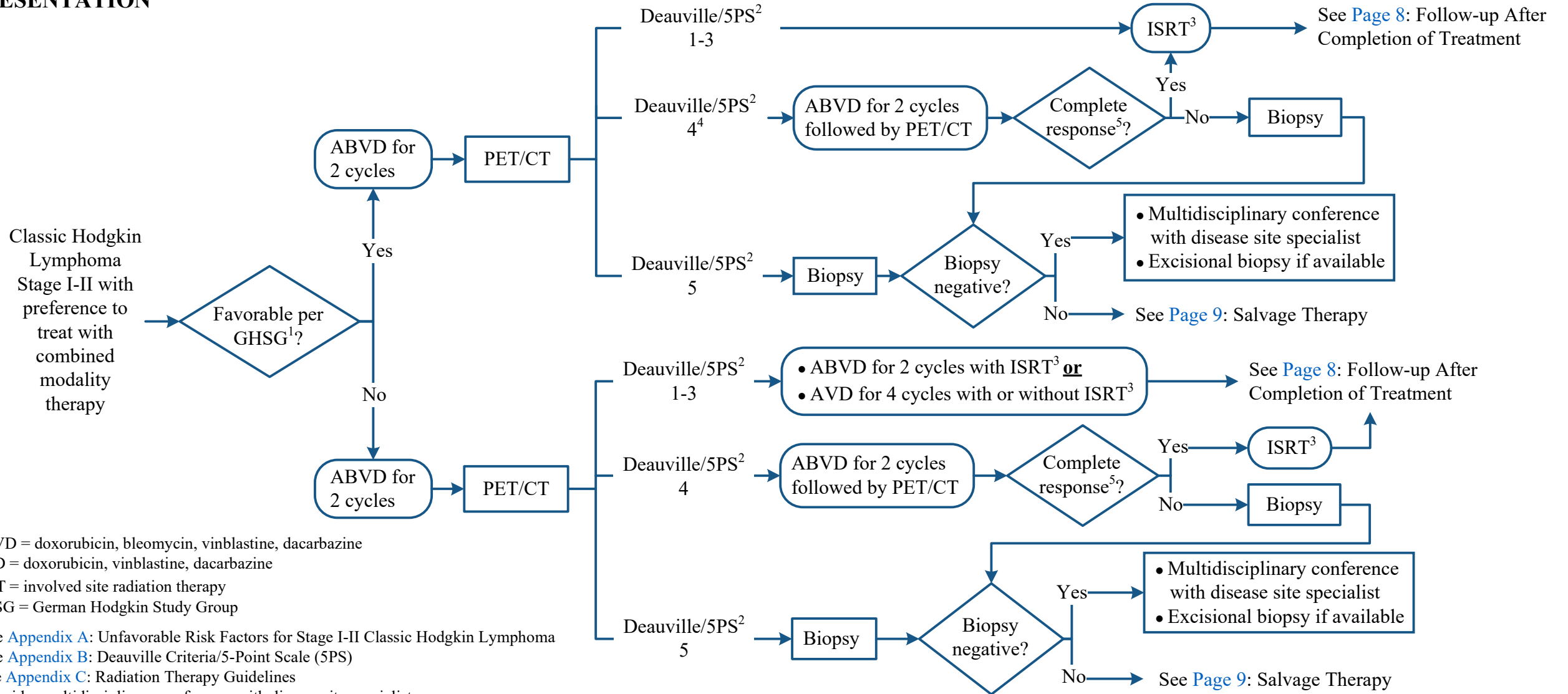
NOTE: Consider Clinical Trials as treatment options for eligible patients.

CLINICAL PRESENTATION

PRIMARY TREATMENT

RESPONSE EVALUATION

TREATMENT



ABVD = doxorubicin, bleomycin, vinblastine, dacarbazine

AVD = doxorubicin, vinblastine, dacarbazine

ISRT = involved site radiation therapy

GHSG = German Hodgkin Study Group

¹ See [Appendix A](#): Unfavorable Risk Factors for Stage I-II Classic Hodgkin Lymphoma

² See [Appendix B](#): Deauville Criteria/5-Point Scale (5PS)

³ See [Appendix C](#): Radiation Therapy Guidelines

⁴ Consider multidisciplinary conference with disease site specialist

⁵ For response assessment, refer to: Cheson, B. D., Fisher, R. I., Barrington, S. F., Cavalli, F., Schwartz, L. H., Zucca, E., & Lister, T. A. (2014). Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: The Lugano classification. *Journal of Clinical Oncology*, 32(27), 3059-3067. doi:10.1200/JCO.2013.54.8800

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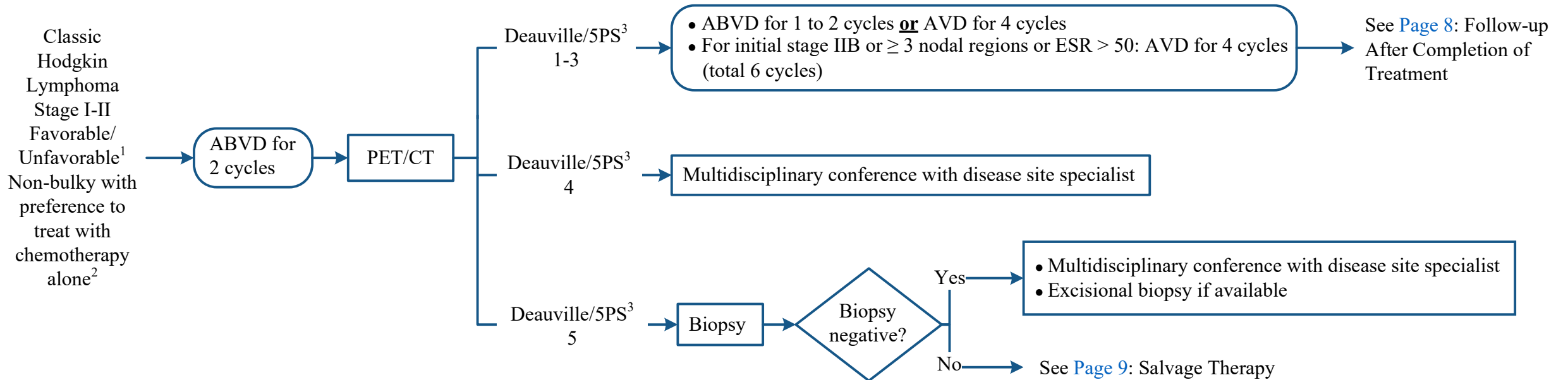
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CLINICAL PRESENTATION

PRIMARY TREATMENT

RESPONSE EVALUATION

TREATMENT



ABVD = doxorubicin, bleomycin, vinblastine, dacarbazine
 AVD = doxorubicin, vinblastine, dacarbazine

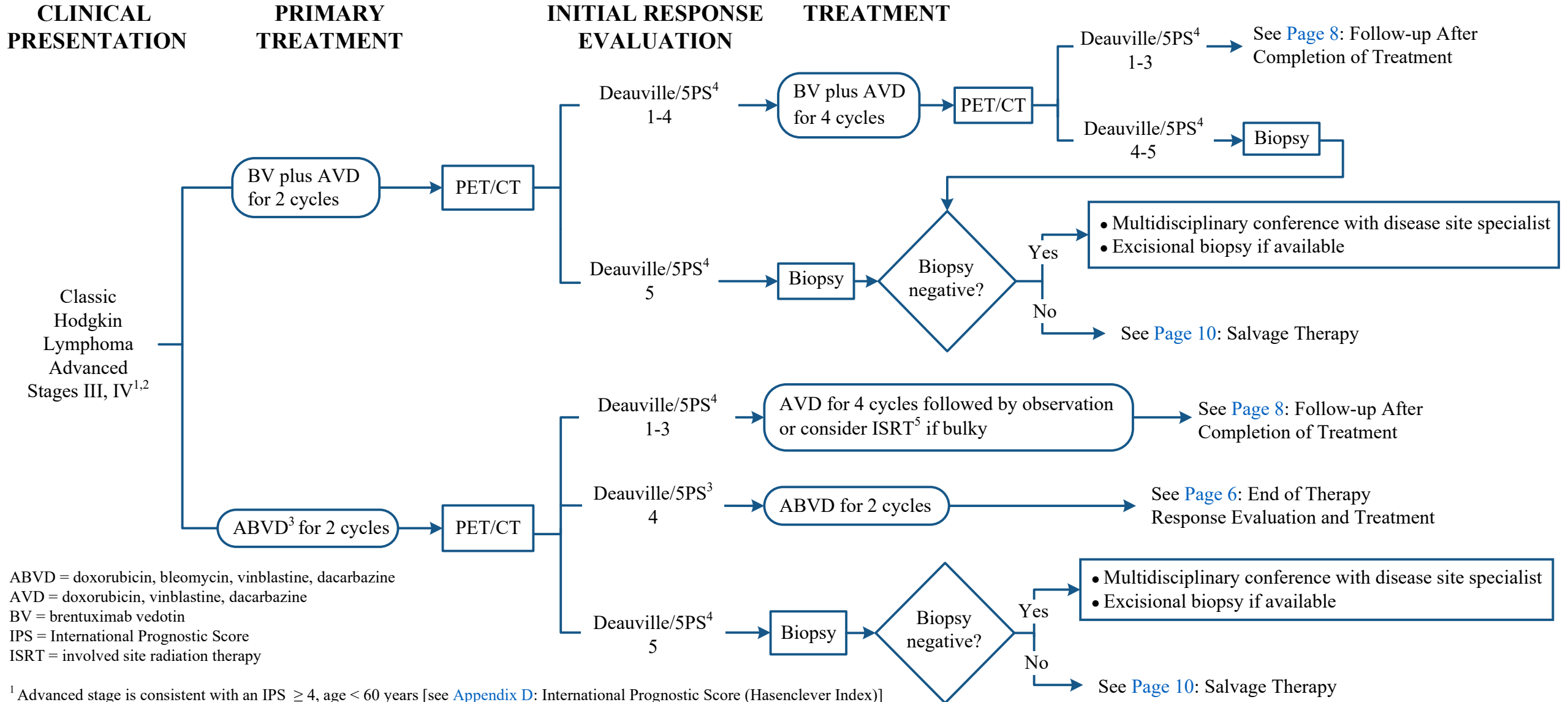
¹ See [Appendix A](#): Unfavorable Risk Factors for Stage I-II Classic Hodgkin Lymphoma

² A subset of patients who meet criteria as per the UK Rapid study with stage IA and stage IIA Hodgkin Lymphoma with no mediastinal bulk and negative PET findings after treatment may receive 3 cycles of chemotherapy with or without additional involved site radiation therapy (ISRT)

³ See [Appendix B](#): Deauville Criteria/5-Point Scale (5PS)

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ABVD = doxorubicin, bleomycin, vinblastine, dacarbazine
 AVD = doxorubicin, vinblastine, dacarbazine
 BV = brentuximab vedotin
 IPS = International Prognostic Score
 ISRT = involved site radiation therapy

¹ Advanced stage is consistent with an IPS ≥ 4 , age < 60 years [see Appendix D: International Prognostic Score (Hasenclever Index)]

² Choice of regimen is based on IPS, comorbidities and physician discretion

³ Patients with IPS ≥ 4 and age < 65 years may benefit from BV plus AVD. Patients with underlying neuropathy should proceed with caution. Patients who are at higher risk for bleomycin lung toxicity should be considered for BV plus AVD.

⁴ See Appendix B: Deauville Criteria/5-Point Scale (5PS)

⁵ See Appendix C: Radiation Therapy Guideline

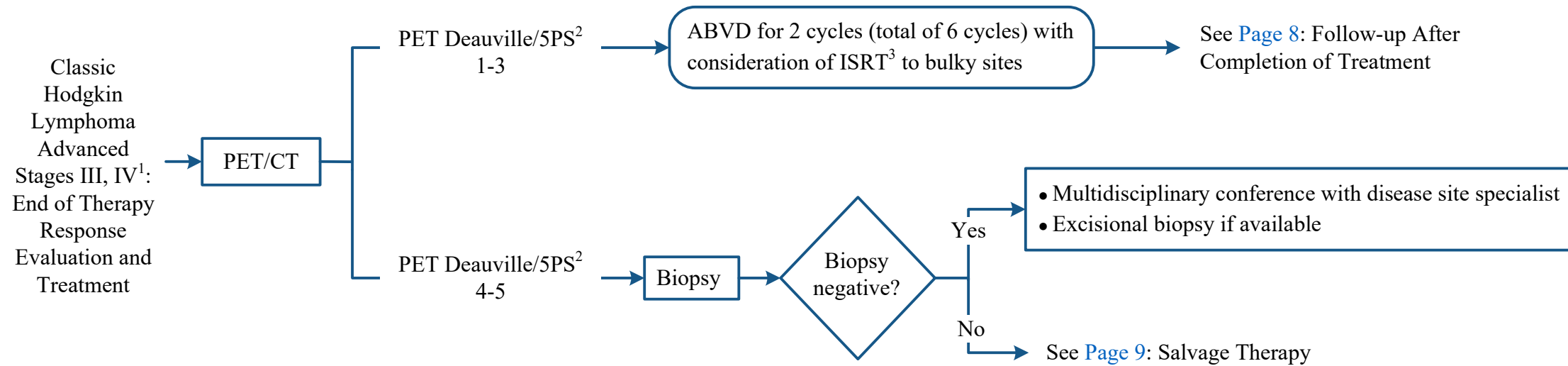
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CLINICAL PRESENTATION

RESPONSE EVALUATION

TREATMENT



ABVD = doxorubicin, bleomycin, vinblastine, dacarbazine
 ISRT = involved site radiation therapy

¹ Advanced stage is consistent with an International Prognostic Score ≥ 4 , age < 60 [see [Appendix D](#): International Prognostic Score (Hasenclever Index)]

² See [Appendix B](#): Deauville Criteria/5-Point Scale (5PS)

³ See [Appendix C](#): Radiation Therapy Guideline

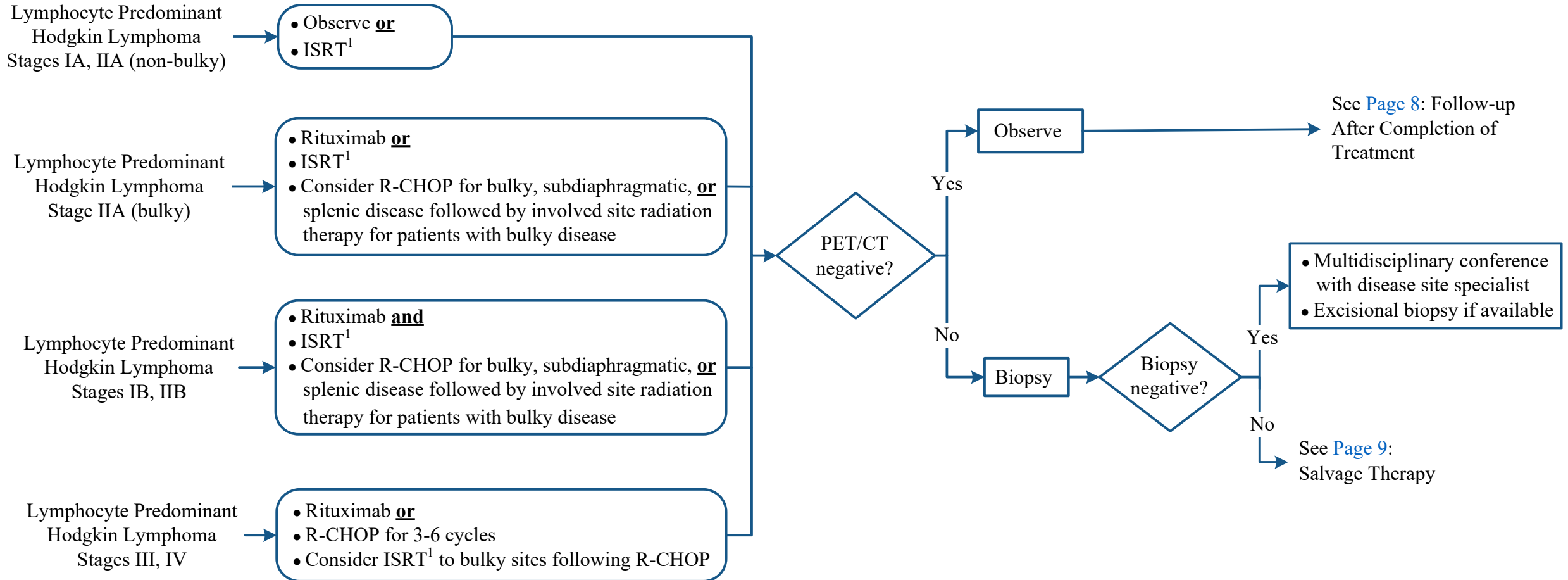
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CLINICAL PRESENTATION

PRIMARY TREATMENT

INITIAL RESPONSE EVALUATION



ISRT = involved site radiation therapy
 R-CHOP = rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone

¹ See [Appendix C: Radiation Therapy Guideline](#)

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FOLLOW-UP AFTER COMPLETION OF TREATMENT

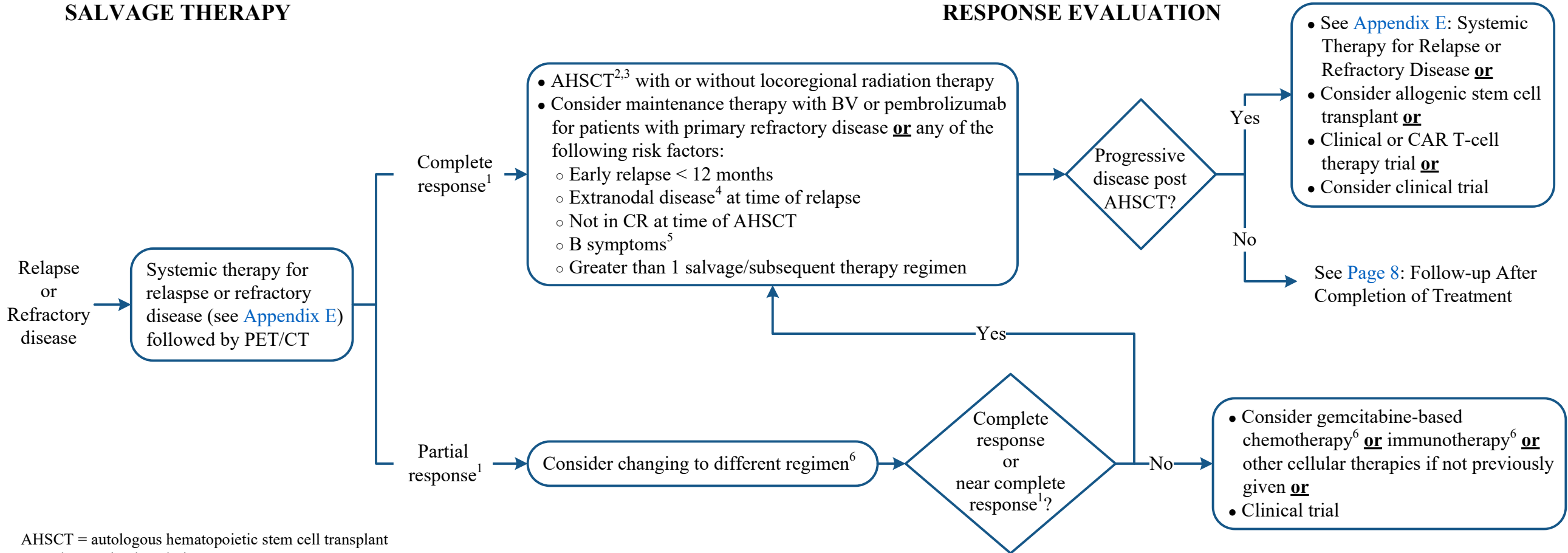
- Follow-up with an oncologist is recommended
- Interim history and physical: every 4 months for years 1 and 2, then every 6 months for year 3, then annually
- Pneumococcal and meningococcal revaccination if patient treated with splenic radiation therapy. See [Management of Adult Asplenic/Hyposplenic Patients algorithm](#).
- Annual influenza vaccine (especially if patient treated with bleomycin or chest radiation therapy)
- Laboratory studies:
 - CBC with differential, LDH, BUN, creatinine, albumin, AST, ALT, total bilirubin, alkaline phosphatase, serum calcium, uric acid every 4 months for years 1 and 2, then every 6 months for years 3, then annually
 - TSH every 6 months if radiation therapy to neck and optional for all other cases
- CT neck, chest, abdomen and pelvis with contrast at 6, 12, and 24 months or as clinically indicated. PET/CT only if last PET was Deauville/5PS 4-5, to confirm complete response
- Annual breast screening: If radiation therapy to the chest or axilla, initiate breast screening 8 years post therapy or at age 40 years, whichever is sooner. If radiation therapy was given between the ages of 10 and 30 years, breast MRI should be performed in addition to mammography.
- Counseling: reproduction, health habits, psychosocial, cardiovascular, breast self-exam, skin cancer risk, end-of-treatment discussion
- Recommend written follow-up instructions for the patient
- Stress test/echocardiogram at 10-year intervals after treatment is completed
- Consider carotid ultrasound at 10-year intervals if neck irradiation

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SALVAGE THERAPY

RESPONSE EVALUATION



AHSCT = autologous hematopoietic stem cell transplant
 BV = brentuximab vedotin
 CAR = chimeric antigen receptor

¹ For response assessment, refer to: Cheson, B. D., Fisher, R. I., Barrington, S. F., Cavalli, F., Schwartz, L. H., Zucca, E., & Lister, T. A. (2014). Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: The Lugano classification. *Journal of Clinical Oncology*, 32(27), 3059-3067. doi: 10.1200/JCO.2013.54.8800

² Conventional-dose chemotherapy may precede high-dose therapy. Sequence of therapy may vary.

³ Perform biopsy if plan to treat with high-dose chemotherapy

⁴ Extranodal disease (*i.e.*, any tumor spread that involves tissues other than those of the lymph nodes, spleen, thymus, Waldeyer's tonsillar ring, appendix, and Peyer's patches)

⁵ Unexplained fever > 38°C during the previous month, recurrent drenching night sweats during the previous month, weight loss > 10% of body weight ≤ 6 months of diagnosis

⁶ See Appendix E: Systemic Therapy for Relapse or Refractory Disease

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APPENDIX A: Unfavorable Risk Factors for Stage I-II Classic Hodgkin Lymphoma

Risk Factor	GHSG	EORTC	NCCN
Age		≥ 50	
Histology			
ESR and B symptoms ¹	ESR > 50 mm/hour if A; ESR > 30 mm/hour if B	ESR > 50 mm/hour if A; ESR > 30 mm/hour if B	ESR ≥ 50 mm/hour or any B symptoms ¹
Mediastinal mass	MMR > 0.33	MTR > 0.35	MMR > 0.33
# Nodal sites	Area ≥ 3 ²	Sites > 3 ²	Sites > 3
E lesion	any		
Bulky ³			Size > 10 cm

A = no B symptoms

GHSG = German Hodgkin Study Group

EORTC = European Organization for the Research and Treatment of Cancer

MMR = Mediastinal mass ratio, maximum width of mass/maximum intrathoracic diameter

MTR = Mediastinal thoracic ratio, maximum width of mediastinal mass/intrathoracic diameter at T5-6

NCCN = National Comprehensive Cancer Network

¹ Unexplained fever > 38°C during the previous month, recurrent drenching night sweats during the previous month, weight loss > 10% of body weight ≤ 6 months of diagnosis

² The EORTC includes the infraclavicular/subpectoral area with the axilla area while the GHSG includes this area with the cervical. Both EORTC and GHSG combine the mediastinum and bilateral hila as a single region.

³ Bulky may be defined as MMR > 0.33 **or** any mass >10 cm in size

APPENDIX B: Deauville Criteria/5-Point Scale (5PS)

- Score 1: no uptake
- Score 2: uptake less than or equal to mediastinum
- Score 3: uptake greater than mediastinum but less than or equal to liver
- Score 4: uptake moderately greater than liver
- Score 5: uptake markedly greater than liver and/or new sites of disease
- Score X: new areas of uptake unlikely to be related to lymphoma

A Deauville Criteria/5PS score of 1-3 is regarded as negative and 4 or 5 as positive

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APPENDIX C: Radiation Therapy Guidelines

Consider intensity-modulated radiation therapy (IMRT) or proton therapy, as appropriate, to minimize toxicity

Dose if radiation therapy is given alone:

30-45 Gy, depending on treatment intent, disease bulk, *etc.*

Doses for combined modality radiation therapy:

- Early stage favorable: 20 Gy to involved site
- Early stage unfavorable: 30 Gy to involved site

Salvage radiation therapy when Deauville/5PS ≥ 4 ¹:

36-45 Gy, depending on disease bulk and response to chemotherapy

Radiation Fields:

Involved Site Radiation Therapy: Treatment of involved lymph nodes regions only

¹ See [Appendix B](#): Deauville Criteria/5-Point Scale (5PS)

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APPENDIX D: International Prognostic Score (Hasenclever Index¹)

- Albumin < 4 g/dL
- Hemoglobin < 10.5 g/dL
- Male
- Age ≥ 45 years
- Stage IV disease
- White blood cell count ≥ 15 K/microliter
- Lymphocyte count < 8% of white blood cell count, and/or lymphocyte count < 0.6 K/microliter)

Each factor = 1 point

¹ Hasenclever, D., Diehl, V., Armitage, J. O., Assouline, D., Björkholm, M., Brusamolino, E., ... Eghbali, H. (1998).

A prognostic score for advanced Hodgkin's disease. *New England Journal of Medicine*, 339(21), 1506-1514. doi:10.1056/NEJM199811193392104

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APPENDIX E: Systemic Therapy for Relapsed or Refractory Disease

Disease	Chemotherapy Options	Subsequent Options ¹
Classic Hodgkin Lymphoma	<ul style="list-style-type: none"> • Brentuximab vedotin • Brentuximab vedotin plus bendamustine • Brentuximab vedotin plus nivolumab • DHAP (dexamethasone, cisplatin, high dose cytarabine) • ESHAP (etoposide, methylprednisolone, high dose cytarabine, cisplatin) • Gemcitabine/bendamustine/vinorelbine • GVD (gemcitabine, vinorelbine, liposomal doxorubicin) • ICE (ifosfamide, carboplatin, etoposide) • IGEV (ifosfamide, gemcitabine, vinorelbine) • Pembrolizumab plus GVD (gemcitabine, vinorelbine, liposomal doxorubicin) • Pembrolizumab for patients not eligible for stem cell transplant 	<ul style="list-style-type: none"> • Bendamustine • Everolimus • GCD (gemcitabine, carboplatin, dexamethasone) • Lenalidomide • MINE (etoposide, ifosfamide, mesna, mitoxantrone) • Mini-BEAM (carmustine, cytarabine, etoposide, melphalan) • Nivolumab • Pembrolizumab
Lymphocyte Predominant Hodgkin Lymphoma	<ul style="list-style-type: none"> • Rituximab plus DHAP (dexamethasone, cisplatin, high dose cytarabine) • Rituximab plus ESHAP (etoposide, methylprednisolone, high dose cytarabine, cisplatin) • Rituximab plus ICE (ifosfamide, carboplatin, etoposide) • Rituximab plus IGEV (ifosfamide, gemcitabine, vinorelbine) 	

¹ Subsequent options also include chemotherapy options that were not previously given

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DEVELOPMENT CREDITS

This practice algorithm is based on majority expert opinion of the Lymphoma Center Faculty at the University of Texas MD Anderson Cancer Center. It was developed using a multidisciplinary approach that included input from the following:

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